APPENDIX D

BACKGROUND ON RISK ASSESSMENT FOR SCREEN RECLAMATION PROCESSES: SCREEN PRINTING CTSA

HUMAN HEALTH RISK

Assessment of the human health risks presented by chemical substances includes the following components of analysis:

- **Hazard Identification** is the process of determining whether exposure to a chemical can cause an adverse health effect and whether the adverse health effect is likely to occur in humans.

- **Dose-response Assessment** is the process of defining the relationship between the dose of a chemical received and the incidence of adverse health effects in the exposed population. From the quantitative dose-response relationship, toxicity values are derived that are used in the risk characterization step to estimate the likelihood of adverse effects occurring in humans at different exposure levels.

- **Exposure Assessment** identifies populations exposed to a chemical, describes their composition and size, and presents the types, magnitudes, frequencies, and durations of exposure to the chemical.

- **Risk Characterization** integrates hazard and exposure information into quantitative and qualitative expressions of risk. A risk characterization includes a description of the assumptions, scientific judgments, and uncertainties embodied in the assessment.

Quantitative Expressions of Hazard and Risk

The manner in which estimates of hazard and risk are expressed depends on the nature of the hazard and the types of data upon which the assessment is based. For example, cancer risks are most often expressed as the probability of an individual developing cancer over a lifetime of exposure to the chemical in question. Risk estimates for adverse effects other than cancer are usually expressed as the ratio of a toxicologic potency value to an estimated dose or exposure level. A key distinction between cancer and other toxicologic effects is that most carcinogens are assumed to have no dose threshold; that is, no dose or exposure level can be presumed to be without some risk. Other toxicologic effects are generally assumed to have a dose threshold; that is, a dose or exposure level below which a significant adverse effect is not expected.

Cancer Hazard and Risk

EPA employs a "weight-of-evidence" approach to determine the likelihood that a chemical is a human carcinogen.[1] Each chemical evaluated is placed into one of the five weight-of-evidence categories listed below.

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[1] The "Proposed Guidelines for Carcinogen Risk Assessment" (EPA, 1996b) propose use of weight-of-evidence descriptors, such as "Likely" or "Known," "Cannot be determined," and "Not likely," in combination with a hazard narrative, to characterize a chemical's human carcinogenic potential - rather than the classification system described above.

- Group A - human carcinogen;
- Group B - probable human carcinogen. B1 indicates limited human evidence; B2 indicates sufficient evidence in animals and inadequate or no evidence in humans;
- Group C - possible human carcinogen;
- Group D - not classifiable as to human carcinogenicity; and
- Group E - evidence of noncarcinogenicity for humans.

When the available data are sufficient for quantitation, EPA develops an estimate of the chemical's carcinogenic potency. EPA "slope factors" express carcinogenic potency in terms of the estimated upper-bound incremental lifetime risk per mg/kg average daily dose. "Unit risk" is a similar measure of potency for air or drinking water concentrations and is expressed as risk per $\mu g/m^3$ in air or as risk per µg/l in water for continuous lifetime exposures.

Cancer risk is calculated by multiplying the estimated dose or exposure level by the appropriate measure of carcinogenic potency. For example an individual with a lifetime average daily dose of 0.3 mg/kg of a carcinogen with a potency of 0.02/mg/kg/day would experience a lifetime cancer risk of 0.006 from exposure to that chemical. In general, risks from exposures to more than one carcinogen are assumed to be additive, unless other information points toward a different interpretation.

Chronic Health Risks

Because adverse effects other than cancer and gene mutations are generally assumed to have a dose or exposure threshold, a different approach is needed to evaluate toxicologic potency and risk for these "systemic effects." "Systemic toxicity" means an adverse effect on any organ system following absorption and distribution of a toxicant to a site in the body distant from the toxicant's entry point. EPA uses the "Reference Dose" approach to evaluate chronic (long-term) exposures to systemic toxicants. The Reference Dose (RfD) is defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime" and is expressed as a mg/kg/day dose. The RfD is usually based on the most sensitive known effect; that is, the effect that occurs at the lowest dose . EPA calculates a comparable measure of potency for continuous inhalation exposures called a Reference Concentration or RfC, expressed as a mg/m^3 air concentration. Although some RfDs and RfCs are based on actual human data, they are most often calculated from results obtained in chronic or subchronic animal studies. The basic approach for deriving an RfD or RfC involves determining a "no-observed-adverse-effect level (NOAEL)" or "lowest-observed-adverse-effect level (LOAEL)" from an appropriate toxicologic or epidemiologic study and then applying various uncertainty factors and modifying factors to arrive at the RfD/RfC.

RfDs and RfCs can be used to evaluate risks from chronic exposures to systemic toxicants. EPA defines an expression of risk called a "Hazard Quotient" which is the ratio of the estimated chronic dose/exposure level to the RfD/RfC. Hazard Quotient values below unity imply that adverse effects are very unlikely to occur. The greater the Hazard Quotient exceeds unity, the greater is the level of concern. However, it is important to remember that the Hazard

Quotient is not a probabilistic statement of risk. A quotient of 0.001 does not mean that there is a one-in-a-thousand chance of the effect occurring. Furthermore, it is important to remember that the level of concern does not necessarily increase linearly as the quotient approaches or exceeds unity because the RfD/RfC does not provide any information about the shape of the dose-response curve.

An expression of risk that can be used when an RfD/RfC is not available is the "Margin-of-Exposure (MOE)." The MOE is the ratio of a NOAEL or LOAEL (preferably from a chronic study) to an estimated dose or exposure level. Very high MOE values such as values greater than 100 for a NOAEL-based MOE or 1000 for a LOAEL-based MOE imply a very low level of concern. As the MOE decreases, the level of concern increases. As with the Hazard Quotient, it is important to remember that the MOE is not a probabilistic statement of risk.

Developmental Toxicity Risks

Because of the many unique elements associated with both the hazard and exposure components of developmental toxicity risk assessment, these risks are treated separately from other systemic toxicity risks.

EPA defines developmental toxicity as adverse effects on the developing organism that may result from exposure prior to conception, during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency.

There is a possibility that a single exposure may be sufficient to produce adverse developmental effects. Therefore, it is assumed that, in most cases, a single exposure at any of several developmental stages may be sufficient to produce an adverse developmental effect. In the case of intermittent exposures, examination of the peak exposure(s) as well as the average exposure over the time period of exposure is important.

EPA has derived Reference Doses and Reference Concentrations for developmental toxicants in a similar manner to the RfDs and RfCs for other systemic toxicants. The RfD_{DT} or RfC_{DT} is an estimate of a daily exposure to the human population that is assumed to be without appreciable risk of deleterious developmental effects. The use of the subscript DT is intended to distinguish these terms from the more common RfDs and RfCs that refer to chronic exposure situations for other systemic effects.

Developmental toxicity risk can be expressed as a Hazard Quotient (dose or exposure level divided by the RfD_{DT} or RfC_{DT}) or Margin-of-Exposure (NOAEL or LOAEL divided by the dose or exposure level), with careful attention paid to the exposure term, as described above.

NOTE: *The closely related area of reproductive toxicity is also an important aspect of systemic toxicity. For purposes of this report, toxicity information on adult male and female reproductive systems will be assessed as part of the chronic toxicity risk.*

Assumptions and Uncertainties

Estimated doses assume 100 percent absorption. The actual absorption rate may be significantly lower, especially for dermal exposures to relatively polar compounds. The assessment used the most relevant toxicological potency factor available for the exposure under consideration. In some cases the only potency factor available was derived from a study employing a different route of exposure than the exposure being evaluated. For example, oral RfD values were sometimes used to calculate Hazard Quotients for inhalation and dermal exposures. For the occupational risk assessment, RfC values were converted to units of dose assuming a breathing rate of 20 m^3/day and a body weight of 70 kg. This conversion was done because occupational inhalation exposures were calculated as a daily dose rather than as an average daily concentration. The general population risk estimates compare RfC values directly to average daily concentrations because continuous exposure is assumed for the general population. Most of the Margin-of-Exposure calculations presented in the assessment are based on toxicity data that have not been formally evaluated by the Agency. Simple esters of glycol ethers were assumed to present the same hazards at approximately the same potencies as the corresponding alcohol. The same potency data were used in risk estimates for each alcohol and its corresponding ester unless specific data for each compound were available.

All risk estimates are based on release and exposure values estimated from information on product usage and work practices obtained from industry surveys. No actual measures of chemical release or exposure levels were available.

Certain formulation components are described in the CTSA by their category name, such as propylene glycol series ethers. However, all risk calculations in the CTSA are based on chemical-specific hazard and exposure data. Thus, risk values may appear for some category members but not others because of limitations in available data.

ECOLOGICAL RISK

The basic elements of ecological risk assessment are similar to those employed in human health risk assessment. This report will address only ecological risks to aquatic species. Quantitative evaluation of aquatic risks involves deriving an "ecotoxicity concern concentration (ECO CC)" for chronic exposures to aquatic species. The ECO CC may be based either on valid toxicologic test data on the subject chemical or on quantitative structure-activity relation analysis of test data on similar chemicals. The ECO CC is typically expressed as a mg/l water concentration. Concentrations below the ECO CC are assumed to present low risk to aquatic species. A notation of "N.E.S." rather than a numeric estimate of the ECO CC indicates that no adverse effects are expected in a saturated solution during the specified exposure period.